Office Action Dated: December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Previously Presented) A compound of formula

$$\begin{array}{c|c}
R^3 & R^1 & X \\
A & N & N \\
R^4 & N & N
\end{array}$$
(I)

a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof, wherein

ring A represents phenyl;

 R^1 represents hydrogen; aryl; formyl; C_{1-6} alkylcarbonyl; C_{1-6} alkyl; C_{1-6} alkyloxycarbonyl; C_{1-6} alkylsubstituted with formyl, C_{1-6} alkylcarbonyl, C_{1-6} alkyloxycarbonyl,

 $C_{1\text{-}6}$ alkylcarbonyloxy; or $C_{1\text{-}6}$ alkyloxy $C_{1\text{-}6}$ alkylcarbonyl optionally substituted with $C_{1\text{-}6}$ alkyloxycarbonyl;

X represents a direct bond; $-(CH_2)_{n3}$ - or $-(CH_2)_{n4}$ - X_{1a} - X_{1b} -;

with n_3 representing an integer with value 1, 2, 3 or 4; with n_4 representing an integer with value 1 or 2; with X_{1a} representing O, C(=O) or NR⁵; and with X_{1b} representing a direct bond or C_{1-2} alkyl;

R² represents C₃₋₇cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula

wherein -B-C- represents a bivalent radical of formula

$$-CH_2-CH_2-CH_2-$$
 (b-1);

$$-CH_2-CH_2-CH_2-CH_2-$$
 (b-2);

$$-X_1$$
-CH₂-CH₂-(CH₂)_n- (b-3);

$$-X_1$$
-CH₂-(CH₂)_n-X₁- (b-4);

$$-X_1$$
-(CH₂)_n·-CH=CH- (b-5);

$$-CH=N-X_1-$$
 (b-6);

with X_1 representing O or NR⁵;

n representing an integer with value 0, 1, 2 or 3;

n' representing an integer with value 0 or 1;

Page 2 of 15

Application No.: 10/564,844

Office Action Dated: December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

wherein said R² substituent, where possible, may optionally be substituted with at least one substituent selected from halo; hydroxy; C₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkyloxyC₁-4alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkyl-

carbonyloxy, NR^6R^7 , $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n1}-R^8$ or

-NR⁵-S(=O)_{n1}-R⁸; C₂₋₆alkenyl or C₂₋₆alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy,

C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷,

 $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$; polyhalo-

C₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkyloxyC₁₋₄alkyloxy, C₁₋₄alkylcarbonyl,

C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷, -C(=O)-NR⁶R⁷, -NR⁵-C(=O)-NR⁶R⁷. $-S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$; C_{1-6} alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl,

 C_{1-4} alkyloxy, C_{1-4} alkylcarbonyl, C_{1-4} alkyl-oxycarbonyl, C_{1-4} alkylcarbonyloxy, NR^6R^7 , - $C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$; polyhalo C_{1-} 6 alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkyloxyC₁₋₄alkyloxy,

C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy. NR⁶R⁷.

 $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$;

C₁₋₆alkylthio; polyhaloC₁₋₆alkylthio; C₁₋₆alkyloxycarbonyl; C₁₋₆alkylcarbonyloxy; C₁₋₆ 6alkylcarbonyl; polyhaloC₁₋₆alkylcarbonyl; cyano; carboxyl; NR⁶R⁷; C(=O)NR⁶R⁷; $-NR^5-C(=O)-NR^6R^7$; $-NR^5-C(=O)-R^5$; $-S(=O)_{n1}-R^8$; $-NR^5-S(=O)_{n1}-R^8$; -S-CN; $-NR^5-CN$; aryloxy; arylthio; arylcarbonyl; arylC₁₋₄alkyl; arylC₁₋₄alkyloxy; a 5-or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered monocyclic heterocycle optionally being substituted with at least

one substituent selected from
$$R^9$$
; or ${}^{-(CH_2)_{n2}-X_2-(CH_2)_{n2}-N}$;

with n2 representing an integer with value 0, 1, 2, 3 or 4; with X₂ representing O, NR⁵ or a direct bond; with X₃ representing O, CH₂, CHOH, CH-N(R⁵)₂, NR⁵ or

 $N-C(=O)-C_{1-4}alkyl;$

R³ represents halo; hydroxy; C₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkyloxy-C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR^{6b}R^{7b}, - **DOCKET NO.:** JANS-0090 (PRD2066USPCT) **Application No.:** 10/564,844

Office Action Dated: December 31, 2007

 $C(=O)-NR^{6b}R^{7b}$, $-NR^5-C(=O)-NR^{6b}R^{7b}$, $-S(=O)_{n1}-R^{8a}$ or

 $-NR^5$ -S(=O)_{n1}-R^{8a}; C₂₋₆alkenyl or C₂₋₆alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy,

C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR^{6b}R^{7b},

-C(=O)-NR^{6b}R^{7b}, -NR⁵-C(=O)-NR^{6b}R^{7b}, -S(=O)_{n1}-R^{8a} or -NR⁵-S(=O)_{n1}-R^{8a}; polyhaloC₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkyloxy, C_{1-4} alkyloxy,

C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR^{6b}R^{7b},

 $-C(=O)-NR^{6b}R^{7b}$, $-NR^5-C(=O)-NR^{6b}R^{7b}$, $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$;

 C_{1-6} alkyloxy optionally substituted with one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1

C₁₋₄alkylcarbonyloxy, NR^{6b}R^{7b}, -C(=O)-NR^{6b}R^{7b}, -NR⁵-C(=O)-NR^{6b}R^{7b},

 $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$; polyhalo C_{1-6} alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy,

 $C_{1\text{--}4}$ alkyloxy $C_{1\text{--}4}$ alkyloxy, $C_{1\text{--}4}$ alkyloxycarbonyl, $C_{1\text{--}4}$ alkyloxycarbonyl,

C₁₋₄alkylcarbonyloxy, NR^{6b}R^{7b}, -C(=O)-NR^{6b}R^{7b}, -NR⁵-C(=O)-NR^{6b}R^{7b},

 $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$; C_{1-6} alkylthio; polyhalo C_{1-6} alkylthio;

C₁₋₆alkyloxycarbonyl; C₁₋₆alkylcarbonyloxy; C₁₋₆alkylcarbonyl; polyhalo-

C₁₋₆alkylcarbonyl; cyano; carboxyl; aryloxy; arylthio; arylcarbonyl; NR^{6b}R^{7b};

 $C(=O)-NR^{6b}R^{7b}; -NR^5-C(=O)-NR^{6b}R^{7b}; -NR^5-C(=O)-R^5; -S(=O)_{n1}-R^{8a};$

 $-NR^5-S(=O)_{n1}-R^{8a}$; -S-CN; or -NR⁵-CN;

 R^4 represents hydrogen; halo; hydroxy; $C_{1\text{-4}}$ alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, $C_{1\text{-4}}$ alkyloxy, $C_{1\text{-4}}$ alkyloxycarbonyl, $C_{1\text{-4}}$ alkyloxycarbonyl, $C_{1\text{-4}}$ alkyloxycarbonyloxy, $NR^{10}R^{11}$, $-C(=O)-NR^{10}R^{11}$,

-NR⁵-C(=O)-NR¹⁰R¹¹, -S(=O)_{n1}-R¹² or -NR⁵-S(=O)_{n1}-R¹²; C₂₋₄alkenyl or C₂₋₄alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkylcarbonyloxy, NR¹⁰R¹¹, -C(=O)-NR¹⁰R¹¹, -NR⁵-C(=O)-NR¹⁰R¹¹,

-S(=O)_{n1}-R¹² or -NR⁵-S(=O)_{n1}-R¹²; polyhaloC₁₋₃alkyl; C₁₋₄alkyloxy optionally substituted with carboxyl; polyhaloC₁₋₃alkyloxy; C₁₋₄alkylthio; polyhaloC₁₋₃alkylthio; C₁₋₄alkyloxycarbonyl; C₁₋₄alkylcarbonyloxy;

 $C_{1\text{--}4}$ alkylcarbonyl; polyhalo $C_{1\text{--}4}$ alkylcarbonyl; nitro; cyano; carboxyl; $NR^{10}R^{11}$; $C(=O)NR^{10}R^{11}$; $-NR^5$ -C(=O)- $NR^{10}R^{11}$; $-NR^5$ -C(=O)- R^5 ; -S(=O)_{n1}- R^{12} ;

 $-NR^5-S(=O)_{n1}-R^{12}$; -S-CN; or -NR 5 -CN;

R⁵ represents hydrogen; C₁₋₄alkyl or C₂₋₄alkenyl;

Office Action Dated: December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R⁶ and R⁷ each independently represent hydrogen; cyano; C₁₋₆alkylcarbonyl optionally substituted with C₁₋₄alkyloxy or carboxyl; C₁₋₆alkyloxycarbonyl; C₃₋₇cycloalkylcarbonyl; adamantanylcarbonyl; C₁₋₄alkyloxyC₁₋₄alkyl; C₁₋₄alkyl substituted with C₁₋₄alkyl-NR⁵-; C₁₋₆alkyl optionally substituted with at least one substituent selected from halo, hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, polyhalo-

 C_{1-4} alkyl, C_{1-4} alkyloxy C_{1-4} alkyloxy, $NR^{6a}R^{7a}$, $C(=O)NR^{6a}R^{7a}$ or ; with X_2 representing O, CH_2 , CHOH, $CH-N(R^5)_2$, NR^5 or $N-C(=O)-C_{1-4}$ alkyl;

R^{6a} and R^{7a} each independently represent hydrogen; C₁₋₄alkyl; C₁₋₄alkylcarbonyl or a 5- or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N;

 R^{6b} and R^{7b} each independently represent hydrogen; cyano; C_{1-6} alkylcarbonyl optionally substituted with C_{1-4} alkyloxy or carboxyl; C_{1-6} alkyloxycarbonyl; C_{3-7} cycloalkylcarbonyl; adamantanylcarbonyl; C_{1-4} alkyloxy C_{1-4} alkyl; C_{1-4} alkyl substituted with C_{1-4} alkyl- NR^5 -; C_{1-6} alkyl optionally substituted with at least one substituent selected from halo, hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, polyhalo C_{1-4} alkyl, C_{1-4} alkyloxy- C_{1-4} alkyloxy, $NR^{6c}R^{7c}$ or $C(=O)NR^{6c}R^{7c}$;

 R^{6c} and R^{7c} each independently represent hydrogen; $C_{1\text{--}4}$ alkyl or $C_{1\text{--}4}$ alkylcarbonyl;

 $R^8 \ represents \ C_{1\text{--}4} alkyl \ optionally \ substituted \ with \ hydroxy; \ polyhalo C_{1\text{--}4} alkyl \ or \ NR^6 R^7;$

 R^{8a} represents C_{1-4} alkyl optionally substituted with hydroxy; polyhalo C_{1-4} alkyl or $NR^{6b}R^{7b}$;

 R^9 represents halo; hydroxy; $C_{1\text{-}6}$ alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, $C_{1\text{-}4}$ alkyloxy, $C_{1\text{-}4}$ alkyloxycarbonyl, $C_{1\text{-}4}$ alkyloxycarbonyl, $C_{1\text{-}4}$ alkyloxybonyloxy, NR^6R^7 , $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$; $C_{2\text{-}6}$ alkenyl or $C_{2\text{-}6}$ alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, $C_{1\text{-}4}$ alkyloxy, $C_{1\text{-}4}$ alkyloxycarbonyl,

 $C_{1\text{--}4}$ alkylcarbonyloxy, NR^6R^7 , $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, $-S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$; polyhalo $C_{1\text{--}6}$ alkyl; $C_{1\text{--}6}$ alkyloxy optionally substituted with carboxyl; polyhalo $C_{1\text{--}6}$ alkyloxy; $C_{1\text{--}6}$ alkylthio; polyhalo $C_{1\text{--}6}$ alkylthio;

 $C_{1\text{-}6}$ alkyloxycarbonyl; $C_{1\text{-}6}$ alkylcarbonyloxy; $C_{1\text{-}6}$ alkylcarbonyl; cyano; carboxyl; NR^6R^7 ; $C(=O)NR^6R^7$; $-NR^5$ -C(=O)- NR^6R^7 ; $-NR^5$ -C(=O)- R^5 ; $-S(=O)_{n1}$ - R^8 ;

 $-NR^5-S(=O)_{n1}-R^8$; -S-CN; or -NR⁵-CN;

 R^{10} and R^{11} each independently represent hydrogen; $C_{1\text{-}6}$ alkyl; cyano; $C_{1\text{-}6}$ alkylcarbonyl; $C_{1\text{-}4}$ alkyloxy $C_{1\text{-}4}$ alkyl; or $C_{1\text{-}4}$ alkyl substituted with $C_{1\text{-}4}$ alkyl-NR⁵-;

Application No.: 10/564,844

Office Action Dated: December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

R¹² represents C₁₋₄alkyl or NR¹⁰R¹¹;

n1 represents an integer with value 1 or 2;

aryl represents phenyl or phenyl substituted with at least one substituent selected from halo, C₁₋₆alkyl, C₃₋₇cycloalkyl, C₁₋₆alkyloxy, cyano, nitro, polyhaloC₁₋₆alkyl or polyhaloC₁₋₆alkyloxy.

2. (Previously Presented) The compound according to claim 1 wherein

X represents a direct bond; $-(CH_2)_{n3}$ - or $-(CH_2)_{n4}$ -X_a-X_b-;

with n₃ representing an integer with value 1, 2, 3 or 4;

with n₄ representing an integer with value 1 or 2;

with X_a representing O or NR⁵; and

with X_b representing a direct bond or C₁₋₂alkyl;

R² represents C₃₋₇cycloalkyl; phenyl or a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; or a radical of formula

wherein -B-C- represents a bivalent radical of formula

 $-CH_2-CH_2-CH_2-$ (b-1);

 $-CH_2-CH_2-CH_2-CH_2-$ (b-2);

 $-X_1$ -CH₂-CH₂-(CH₂)_n- (b-3);

 $-X_1$ -CH₂-(CH₂)_n-X₁- (b-4);

 $-X_1$ -(CH₂)_n-CH=CH- (b-5);

with X_1 representing O or NR⁵;

n representing an integer with value 0, 1, 2 or 3;

n' representing an integer with value 0 or 1;

wherein said R² substituent, where possible, may optionally be substituted with at least one substituent selected from halo; hydroxy; C₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, C₁₋₄alkylcarbonyloxy, NR⁶R⁷,

 $-C(=O)-NR^6R^7, -NR^5-C(=O)-NR^6R^7, -S(=O)_{n1}-R^8 \text{ or } -NR^5-S(=O)_{n1}-R^8; \ C_{2-6} \text{alkenyl or } \\ C_{2-6} \text{alkynyl, each optionally substituted with at least one substituent selected from } \\ \text{hydroxy, cyano, carboxyl, } C_{1-4} \text{alkyloxy, } C_{1-4} \text{alkylcarbonyl, } C_{1-4} \text{alkyloxycarbonyl, } C_{1-4} \text{alkylcarbonyloxy, } NR^6R^7, -C(=O)-NR^6R^7, -NR^5-C(=O)-NR^6R^7, -S(=O)_{n1}-R^8 \text{ or } -NR^5-S(=O)_{n1}-R^8; \text{ polyhalo} C_{1-6} \text{alkyl; } C_{1-6} \text{alkyloxy optionally substituted with carboxyl; } \\ \text{hydroxyoptionally substituted with carboxyl; } C_{1-6} \text{alkyloxy optionally substituted with carboxyl; } C_{1-6} \text{alkyloxyoptionally substituted with carboxyl; } \\ \text{hydroxyoptionally substituted with carboxyl; } C_{1-6} \text{alkyloxyoptionally substituted with carboxyliked with carbox$

Application No.: 10/564,844

Office Action Dated: December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

polyhaloC₁₋₆alkyloxy; C₁₋₆alkylthio; polyhaloC₁₋₆alkylthio;

C₁₋₆alkyloxycarbonyl; C₁₋₆alkylcarbonyloxy; C₁₋₆alkylcarbonyl;

polyhalo C_{1-6} alkylcarbonyl; cyano; carboxyl; NR^6R^7 ; $C(=O)NR^6R^7$; $-NR^5-C(=O)-NR^6R^7$; $-NR^5-C(=O)-R^5$; $-S(=O)_{n1}-R^8$; $-NR^5-S(=O)_{n1}-R^8$;

-S-CN; -NR⁵-CN; aryloxy; arylthio; arylcarbonyl; arylC₁₋₄alkyl; arylC₁₋₄alkyloxy; a 5-or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered monocyclic heterocycle optionally being substituted

with at least one substituent selected from R^9 ; or

with n2 representing an integer with value 0, 1, 2, 3 or 4;

with X₂ representing O, NR⁵ or a direct bond;

with X₃ representing O or NR⁵;

 R^3 represents halo; hydroxy; $C_{1\text{-}6}$ alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, $C_{1\text{-}4}$ alkyloxy, $C_{1\text{-}4}$ alkyloxycarbonyl, $C_{1\text{-}4}$ alkyloxycarbonyloxy, $C_{1\text{-}4}$ alkyloxycarbonyl, $C_{1\text{-}4}$ alkyloxycarbonyloxy, $C_{1\text{-}4}$

-NR⁵-C(=O)-NR^{6b}R^{7b}, -S(=O)_{n1}-R^{8a} or -NR⁵-S(=O)_{n1}-R^{8a}; C_{2-6} alkenyl or C_{2-6} alkynyl, each optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, C_{1-4} alkyloxycarbonyl,

C₁₋₄alkylcarbonyloxy, NR^{6b}R^{7b}, -C(=O)-NR^{6b}R^{7b}, -NR⁵-C(=O)-NR^{6b}R^{7b},

 $-S(=O)_{n1}-R^{8a}$ or $-NR^5-S(=O)_{n1}-R^{8a}$; polyhalo C_{1-6} alkyl; C_{1-6} alkyloxy optionally substituted with carboxyl; polyhalo C_{1-6} alkyloxy; C_{1-6} alkylthio; polyhalo C_{1-6} alkylthio; C_{1-6} alkylthio; C_{1-6} alkylthio; C_{1-6} alkylthio; C_{1-6} alkylthio; C_{1-6} alkylthio;

6alkyloxycarbonyl; C₁₋₆alkylcarbonyloxy; C₁₋₆alkyl-

carbonyl; polyhalo $C_{1\text{--}6}$ alkylcarbonyl; nitro; cyano; carboxyl; $NR^{6b}R^{7b}$; $C(=O)NR^{6b}R^{7b}$;

 $-NR^5-C(=O)-NR^{6b}R^{7b}; \ -NR^5-C(=O)-R^5; \ -S(=O)_{n1}-R^{8a};$

 $-NR^5-S(=O)_{n1}-R^{8a}$; -S-CN; or -NR⁵-CN;

R⁵ represents hydrogen or C₁₋₄alkyl;

R⁶ and R⁷ each independently represent hydrogen; cyano; C₁₋₆alkylcarbonyl;

 C_{14} alkyloxy C_{1-4} alkyl; C_{1-4} alkyl substituted with C_{1-4} alkyl-NR 5 -; C_{1-6} alkyl optionally substituted with hydroxy, C_{1-4} alkyloxy, C_{1-4} alkyloxy, NR 6a R 7a , C(=O)NR 6a R 7a

or X_4 ; with X_4 representing O or NR⁵;

R^{6a} and R^{7a} each independently represent hydrogen; C₁₋₄alkyl; C₁₋₄alkylcarbonyl or a 5- or 6-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N;

Application No.: 10/564,844

Office Action Dated: December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

 R^{6b} and R^{7b} each independently represent hydrogen; cyano; $C_{1\text{-}6}$ alkylcarbonyl; $C_{1\text{-}4}$ alkyloxy $C_{1\text{-}4}$ alkyl; $C_{1\text{-}4}$ alkyl substituted with $C_{1\text{-}4}$ alkyl-NR⁵-; $C_{1\text{-}6}$ alkyl optionally substituted with hydroxy, $C_{1\text{-}4}$ alkyloxy, $C_{1\text{-}4}$ alkyloxy, $NR^{6a}R^{7a}$ or $C(=O)NR^{6a}R^{7a}$:

R⁸ represents C₁₋₄alkyl, polyhaloC₁₋₄alkyl or NR⁶R⁷; R^{8a} represents C₁₋₄alkyl, polyhaloC₁₋₄alkyl or NR^{6b}R^{7b}.

3. (Previously Presented) The compound according to claim 1 wherein R^1 represents hydrogen; X represents a direct bond or $-(CH_2)_{n3}$ -; R^2 represents phenyl or a radical of formula (b-4), wherein said R^2 may optionally be substituted with at least one substituent, in particular 1, 2 or 3 substituents, selected from halo; C_{1-6} alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, NR^6R^7 , $C(=O)NR^6R^7$, C_{1-4} alkyloxy or C_{1-4} alkyloxy; C_{1-6} alkyloxy;

C₁₋₆alkyloxycarbonyl; C₁₋₄alkyloxyC₁₋₆alkyloxy; cyano; carboxyl; C(=O)NR⁶R⁷;

-S(=O)_{n1}-R⁸; arylC₁₋₄alkyloxy; or a 5-or 6-membered heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered heterocycle optionally being substituted with at least one substituent selected from R⁹; R³ represents halo; hydroxy; C₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, NR^{6b}R^{7b} or C(=O)NR^{6b}R^{7b};

 $C_{2\text{-}6}$ alkenyl optionally substituted with at least one substituent selected from carboxyl or $C_{1\text{-}4}$ alkyl-oxycarbonyl; polyhalo $C_{1\text{-}6}$ alkyloxy; $C_{1\text{-}6}$ alkyloxy optionally substituted with $C_{1\text{-}4}$ alkyloxy; $C_{1\text{-}6}$ alkyloxycarbonyl; $C_{1\text{-}6}$ alkylcarbonyl; cyano; carboxyl; $NR^{6b}R^{7b}$; $C(=O)NR^{6b}R^{7b}$; $-NR^5$ -C(=O)- R^5 ; $-S(=O)_{n1}$ - R^8 ; $-NR^5$ - $S(=O)_{n1}$ - R^8 ; or -S-CN; R^4 represents hydrogen; halo; $C_{1\text{-}6}$ alkyl; cyano; hydroxy; $C_{1\text{-}6}$ alkyloxycarbonyl; $C_{1\text{-}6}$ alkyloxy; carboxyl; or NR^6R^7 .

4. (Previously Presented) The compound according to claim 1 wherein-R¹ represents hydrogen; X represents a direct bond; R² represents phenyl wherein said R² may optionally be substituted with at least one substituent, in particular 1, 2 or 3 substituents, selected from halo; C₁₋₆alkyl substituted with one substituent selected from hydroxy, cyano, NR⁶R⁷, C(=O)NR⁶R⁷, C₁₋₄alkyloxy or C₁₋₄alkyloxyC₁₋₄alkyloxy; C₁₋₆alkyloxy; C₁₋₆alkyloxy; C₁₋₆alkyloxy; C(=O)NR⁶R⁷;

-S(=O)_{n1}-R⁸; or a 5-or 6-membered heterocycle containing at least one heteroatom selected from O, S or N and said 5-or 6-membered heterocycle optionally being substituted with at least one substituent selected from R⁹; R³ represents halo; hydroxy; C_{1-6} alkyl optionally

Application No.: 10/564,844

Office Action Dated: December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C_{1-4} alkyloxy, $NR^{6b}R^{7b}$ or $C(=O)NR^{6b}R^{7b}$; C_{2-6} alkenyl optionally substituted with at least one substituent selected from carboxyl or C_{1-4} alkyloxycarbonyl; polyhalo C_{1-6} alkyloxy; C_{1-6} alkyloxy optionally substituted with

 $C_{1\text{-}4}$ alkyloxy or $NR^{6b}R^{7b}$; $C_{1\text{-}6}$ alkylthio; $C_{1\text{-}6}$ alkyloxycarbonyl; $C_{1\text{-}6}$ alkylcarbonyl; cyano; carboxyl; $NR^{6b}R^{7b}$; $C(=O)NR^{6b}R^{7b}$; $-S(=O)_{n1}$ - R^8 ; $-NR^5$ -C(=O)- R^5 ; or $-NR^5$ - $S(=O)_{n1}$ - R^8 ; R^4 represents hydrogen; halo; $C_{1\text{-}6}$ alkyl; hydroxy; $C_{1\text{-}6}$ alkyloxy; carboxyl; or NR^6R^7 .

- 5. (Previously Presented) The compound according to claim 1 wherein the R³ substituent is linked to ring A in meta position compared to the NR¹ linker.
- 6. (Previously Presented) The compound according to claim 1 wherein the R³ substituent is linked to ring A in para position compared to the NR¹ linker.
- 7. (Previously Presented) The compound according to claim 1 wherein R³ represents NR^{6b}R^{7b}.
- 8. (Previously Presented) The compound according to claim 1 wherein X represents a direct bond.
- 9. (Previously Presented) The compound according to claim 1 wherein R^2 represents C_{3-7} cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula (a-1) wherein said R^2 substituted with at least one substituted from C_{1-6} alkyl substituted with NR^6R^7 ; C_{2-6} alkenyl or C_{2-6} alkynyl, each substituted with NR^6R^7 ; polyhalo C_{1-6} alkyl substituted with NR^6R^7 ; C_{1-6} alkyloxy substituted with NR^6R^7 ; polyhalo C_{1-6} alkyloxy substituted with NR^6R^7 ; or NR^6R^7 .
- 10. (Previously Presented) The compound according to claim 1 wherein R^3 represents C_{1-6} alkyl substituted with $NR^{6b}R^{7b}$; C_{2-6} alkenyl or C_{2-6} alkynyl, each substituted with $NR^{6b}R^{7b}$; polyhalo C_{1-6} alkyl substituted with $NR^{6b}R^{7b}$; C_{1-6} alkyloxy substituted with $NR^{6b}R^{7b}$; or $NR^{6b}R^{7b}$.

Application No.: 10/564,844

Office Action Dated: December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

11. (Previously Presented) The compound according to claim 1 wherein R² represents C₃₋₇cycloalkyl; phenyl; a 4, 5, 6- or 7-membered monocyclic heterocycle containing at least one heteroatom selected from O, S or N; benzoxazolyl or a radical of formula (a-1), wherein said R² substituent is substituted with at least one substituent selected from halo; polyhaloC₁₋₆alkyl optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, C₁₋₄alkyloxy, C₁₋₄alkyloxy-C₁₋₄alkyloxy, C₁₋₄alkyloxy-C₁₋₄alkyloxy, C₁₋₄alkyloxycarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₄alkyloxycarbonyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkyloxycarbonyl, C₁₋₆alkyloxycarbonyl, S₁colonally substituted with at least one substituent selected from hydroxycarbonyl

 $C_{1\text{--}6}$ alkyloxy optionally substituted with at least one substituent selected from hydroxy, cyano, carboxyl, $C_{1\text{--}4}$ alkyloxy, $C_{1\text{--}4}$ alkyloxyC $_{1\text{--}4}$ alkyloxyC $_{1\text{--}4}$ alkyloxyCarbonyl, $C_{1\text{--}4}$ alkyloxycarbonyl, $C_{1\text{--}4}$ alkyloxycarbonyloxy, NR^6R^7 , $-C(=O)-NR^6R^7$, $-NR^5-C(=O)-NR^6R^7$, -C(=O)-NR

 $S(=O)_{n1}-R^8$ or $-NR^5-S(=O)_{n1}-R^8$.

12. (Previously Presented) The compound according to claim 1 wherein the compound is selected from the group consisting of

DOCKET NO.: JANS-0090 (PRD2066USPCT) **Application No.:** 10/564,844 **Office Action Dated:** December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

a pharmaceutically acceptable addition salt, a quaternary amine or a stereochemically isomeric form thereof.

- 13. (Previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the compound of claim 1.
- 14. (Canceled)
- 15. (Canceled)
- 16. (Canceled)
- 17. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as active ingredient a therapeutically effective amount of a compound as claimed in claim 1.
- 18. (Currently Amended) A process for preparing a pharmaceutical composition comprising intimately mixing a therapeutically effective amount of a compound as claimed in claim 1 with a pharmaceutically acceptable carrier.
- 19. (Currently Amended) A process for preparing a compound as claimed in claim 1, comprising
- a) cyclizing an intermediate of formula (II) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,

wherein ring A, R¹ to R⁴ and X are as defined in claim 1;

b) cyclizing an intermediate of formula (II-a) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,

Application No.: 10/564,844

Office Action Dated: December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

$$(II-a) \begin{picture}(10,0) \put(0,0){\line(1,0){150}} \put(0,0){\line(1$$

wherein ring A, R¹ to R³ and X are as defined in claim 1;

c) cyclizing an intermediate of formula (II-b) in the presence of a nitrite salt, a suitable solvent, and a suitable acid,

$$(II-b)$$

wherein ring A, R¹, R³, R⁴ and X are as defined in claim 1;

d) reacting an intermediate of formula (III) with an intermediate of formula (IV) in the presence of a suitable solvent,

wherein ring A, R¹ to R⁴ and X are as defined in claim 1;

e) reacting an intermediate of formula (III') with an intermediate of formula (IV) in the presence of a suitable solvent, and optionally in the presence of a suitable base,

Application No.: 10/564,844

Office Action Dated: December 31, 2007

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

or, optionally, converting compounds of formula (I) into each other following art-known transformations, and further, if desired, converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or into a therapeutically active non-toxic base addition salt by treatment with a base, or conversely, converting the acid addition salt form into the free base by treatment with alkali, or converting the base addition salt into the free acid by treatment with acid; and, optionally, preparing stereochemically isomeric forms, or quaternary amine forms thereof.